

TRANSFORMATION PRODUCTS OF SCLAREOL

IV. STEREOCHEMISTRY AND MASS-SPECTROMETRIC FRAGMENTATION OF SOME BICYCLOHOMOFARNESANE OXIDES

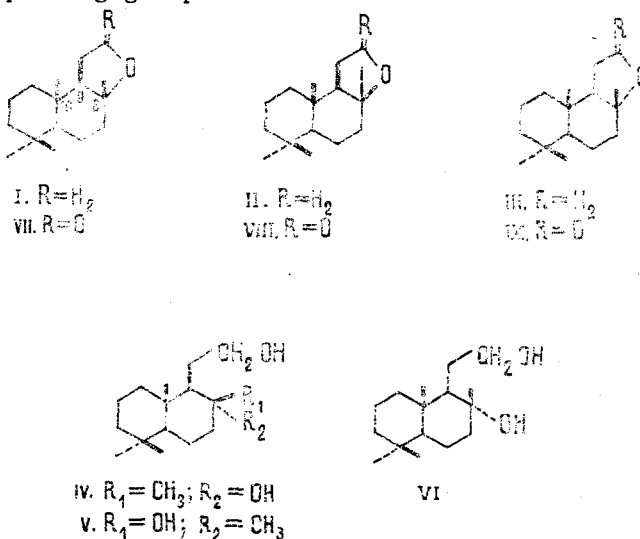
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Among the numerous transformation products of sclareol and of labdane diterpenoids related to it, great interest is presented by the bicyclohomofarnesane oxides (I-III), which possess a powerful ambergris odor [1-3]. Some of them are produced industrially and are used in perfumery as substitutes for ambergris. For example, in the USSR the product "ambroksid," consisting of a mixture of compounds (I) and (II), is used for this purpose [4].

The oxides (I-III) are formed in the dehydration of the glycols (IV-VI). Since the latter were obtained by the reduction of the γ -lactones (VII-IX) by complex aluminum [5] or boron [4, 6] hydrides, their configurations at all the chiral centers are the same as in the corresponding lactones, the stereochemistry of which has been established unambiguously [7]. In its turn, when the diols (IV-VI) are dehydrated only the chiral center at C₈ is affected, i.e., the configurations of the oxides (I-III) and all the asymmetric atoms with the exception of C₈ are identical with the configurations of the same atoms in the initial glycols.

We have directed attention to the fact that although oxides (I) and (II) were synthesized long ago [5, 8, 9], their stereochemistry at C₈ has not been strictly demonstrated. The acid-catalyzed dehydration of the glycol (IV) leads to a mixture of oxides (I) and (II) in which the first of them predominates, and the dehydration of the diastereometric glycol (V) gives a mixture of the same products with the oxide (II) predominating. The predominating dehydration product has been assigned the same configuration at C₈ as the initial diol [9]. However, it is known [10] that under the action of acids the dehydration of 1,4-primary-tertiary diols to the corresponding oxides takes place with the splitting out of the tertiary hydroxyl and the subsequent attack of the carbocation obtained by the primary hydroxy group, i.e., as an S_N1 intramolecular substitution. Consequently, in correspondence with the mechanism of S_N1 substitution [11], in the dehydration of primary-tertiary diols in which the tertiary hydroxy group is attached to a chiral carbon atom and there is no steric hindrance either, equal amounts of the epimeric oxides should be formed or to a certain extent the epimer with the opposite configuration in the chiral center should predominate because of the screening effect of the departing group.



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Although in the bicyclohomofarnesane compounds the β side of the molecule is sterically screened, the available experimental results [9] shows that this does not appreciably affect the course of the splitting out of water from the diols (IV) and (V) since the epimeric oxides predominate in the products of their dehydration.

It follows from what has been said that the predominance of one of the oxides (I) and (II) in the dehydration products of the glycols (IV) and (V) cannot be considered a proof of the identity of the configurations at C_8 in this, the predominating, oxide and in the initial glycol.

The present communication is devoted to establishing the stereochemistry of the oxides (I-III) and to a consideration of the features of their mass-spectrometric behavior.

As was to be expected, in the NMR spectra of compounds (I-III) there are the signals of three methyl groups attached to quaternary carbon atoms and of one attached to a tertiary carbon atom connected with oxide oxygen. In the NMR spectrum of oxide (II), the signal of the methyl at C_{10} shifts downfield in comparison with its position in the spectra of its isomers (I) and (III). This shift can be connected only with the descreening of this methyl group under the influence of the oxide oxygen when they have the 1,3-cis arrangement. Consequently, in compound (II) the oxide oxygen at C_8 is directed axially, and in its isomers (I) and (III) equatorially.

It can be seen from a consideration of the mass spectra of substances (I-III) (Fig. 1) that those of the first two are almost identical. In fact, in the two spectra the maximum peak is that of an ion with m/e 221 ($M - CH_3$), the nominal values of all the peaks are iden-

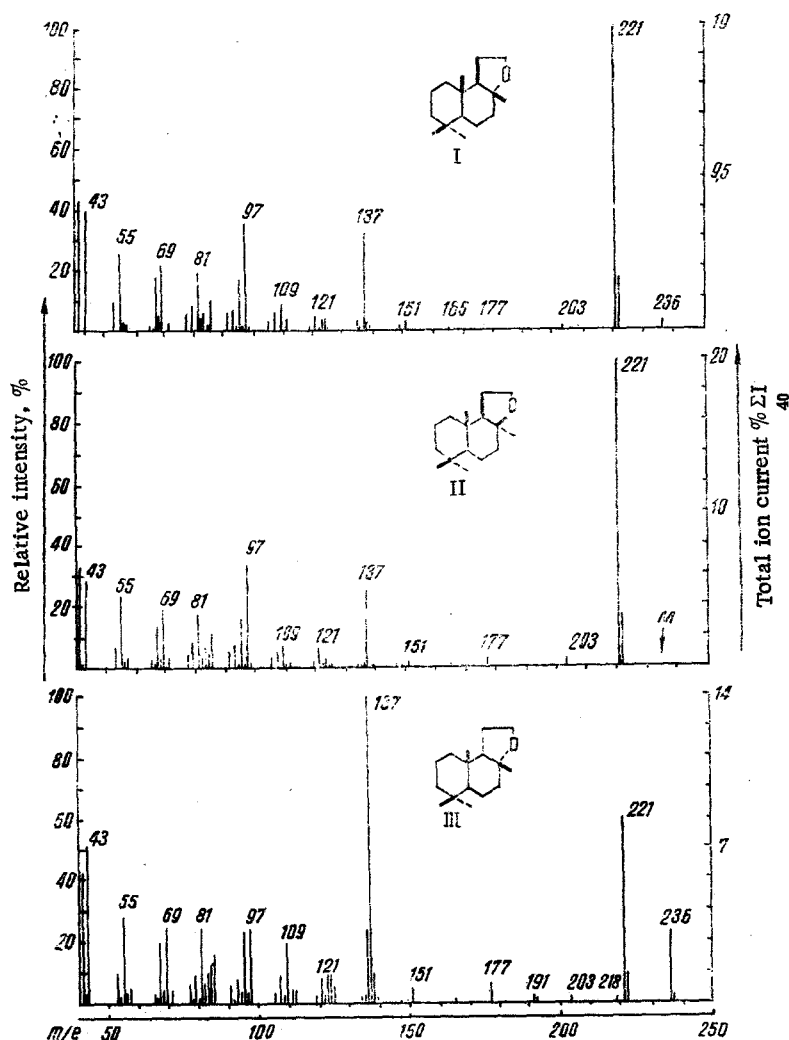
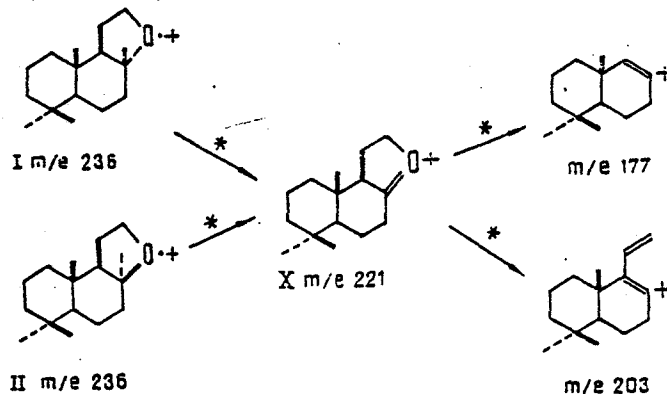


Fig. 1

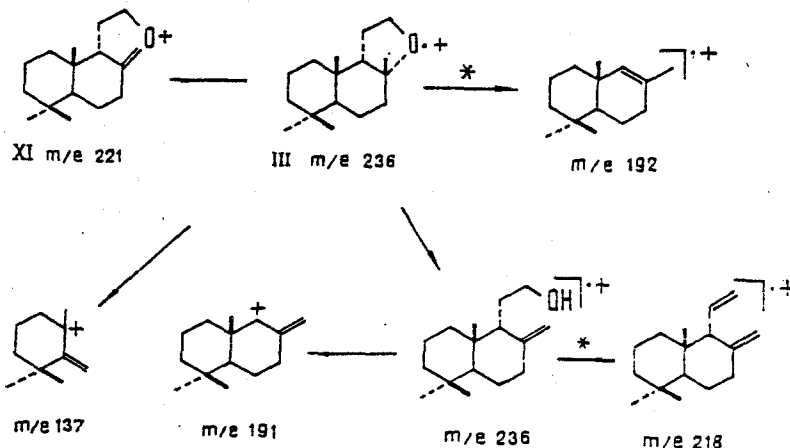
tical, and their intensities, both relative and in fractions of the total ion current, are comparable. The only difference between them is that the mass spectrum of compound (I) contains, in low intensity, the peak of the molecular ion (m/e 236, 2-3%), which is absent from the spectrum of the oxide (II). These facts are explained by the assumption that in the ionization of oxides (I) and (II) under the action of electron impact the predominant localization of the charge on the oxygen atom takes place with the subsequent detachment of the C_8 -methyl group and the formation of the same ion with m/e 221 (X), the subsequent fragmentation of which is monotypical (Scheme 1).



Scheme 1

Thus, with the ejection of the C_8 -methyl group the difference between the fragments that formed the oxides (I) and (II) disappears. This shows that the initial compounds (I) and (II) possess the same configuration at C_9 and are epimeric at C_8 . The presence of the peak of the molecular ion in the spectrum of the oxide (I) and its absence from the spectrum of the oxide (II) reflects the greater stability of the former of them, which should correspond to the trans linkage of ring B and the tetrahydrofuran ring.

The mass spectrum of the oxide (III) differs substantially from the mass spectra of compounds (I) and (II) (see Fig. 1). It contains a fairly strong peak of the molecular ion (23%), the maximum peak that the ion with m/e 137, and the intensity of the peak of the ion with m/e 221 (XI) is only 60% of the maximum. Furthermore, it contains peaks of low intensity with m/e 218, 192, and 191, showing that after ionization in the oxide (III), together with the elimination of the methyl group at C_8 , cleavage of the bond between the oxygen atom and the C_8 carbon atom with the opening of the oxide ring also takes place (Scheme 2).



Scheme 2

Subsequent fragmentation takes place both with the splitting out of a molecule of water and the formation of an ion with m/e 218 and with the splitting out of the side chain, which leads to ions with m/e 192 and 191. It is obvious that the features of the mass spectro-metric fragmentation of the oxide (III) are due to its different configuration at C_9 . The difference that has been observed in the mass spectra of the oxides (I-III) is retained when

the ionizing voltage is reduced from 70 to 20 V. Thus, the conclusions following from the NMR results and from mass spectroscopy are in harmony with one another and confirm the stereochemistry provisionally adopted previously for compounds (I-III).

The stereochemistry of compounds (I-III) was shown definitively by their oxidation under mild conditions with chromium trioxide in acetic acid to the lactones (VII-IX), respectively. In each case, only one oxidation product was formed, i.e., under the given conditions the trans- γ -lactone norambreinolide (VII) is not isomerized into the more stable cis-lactone (VIII).

EXPERIMENTAL

The oxides (I) (mp 74-74.5°C) and (III), n_D^{25} 1.5033, $[\alpha]_D^{23}$ -3.9° (CHCl₃), have been obtained previously. Their isomer (II) (mp 53-54°C) was isolated from ambroksid [4] by chromatography on a column of alumina. According to the literature [8, 9], it melts at 60°C. However, this applies only to those cases when it has been purified by chromatography and has not been recrystallized. We have established that those chromatographic fractions that have mp 60°C actually consist of a mixture of the oxide (II) and a small amount of its epimer (I). The chromatographically pure oxide (II) after recrystallization from CH₃OH melts at 53-54°C.

The mass spectra were recorded on an MKh-1303 instrument fitted with a glass system for introducing the sample directly into the ion source, at a temperature of the evaporator of 20-25°C and of the ionization chamber of 150°C with ionizing voltages of 70 (see Fig. 1) and 20 V. The NMR spectra were taken on an RS-60 instrument in carbon tetrachloride with tetramethylsilane as internal standard, the signals being given in the δ scale, ppm. The signals of the methyl and of the C₁₂-methylene group of compounds (I-III) are given in Table 1.

Oxidation of (I) to (VII). A solution of 46.5 mg of chromic anhydride in 0.35 ml of 90% acetic acid was added to a solution of 50 mg of the oxide (I) in 0.7 ml of glacial acetic acid. The reaction mixture was kept at 50°C for 5 h, diluted with water, and extracted with ether. The extract was washed successively with water, saturated sodium bicarbonate solution, and twice again with water, dried with anhydrous sodium sulfate, and filtered, and the solvent was distilled off. The crystalline residue, an individual substance according to TLC, was twice recrystallized from light petroleum ether, mp 123-124°C. It gave no depression of the melting point in admixture with a sample of norambreinolide (VII). Their IR spectra in carbon tetrachloride were identical.

Oxidation of (II) to (VIII). A solution of 9.3 mg of chromium trioxide in 0.07 ml of 90% acetic acid was added to a solution of 10 mg of the oxide (II) in 0.14 ml of acetic acid, and the reaction mixture was kept at 50°C for 6 h. Then the product was worked up as described above. The crystalline residue (10 mg) gave a single spot on TLC under various conditions, the R_f values of which coincided with those of 8-epinorambreinolide (VIII). After two recrystallizations from light petroleum ether, the product melted at 88-90°C. A mixture with an authentic sample having mp 92-93°C melted at 89-91°C. Their IR spectra, taken in KBr tablets, were identical.

Oxidation of (III) to (IX). The oxide (III) (10 mg) was oxidized and worked up as described for oxide (II). The oxidation product was recrystallized from light petroleum ether, mp 129.5-131°C. A mixture with a sample of 8,9-diepinorambreinolide (IX) with mp 131-132°C melted at 130-131.5°C. Their IR spectra, taken in KBr tablets, were identical.

TABLE 1. Characteristics of the PMR Spectra of Compounds (I)-(III)

Substance	Group. Nature of the signal and its value			
	C ₁₁ -CH ₃ (s)*	C ₄ -(CH ₃) ₂ (s)	C ₈ -CH ₃ (s)	C ₁₂ -CH ₂ (m)*
I	0.82	0.82; 0.87	1.01	3.77
II	0.93	0.94 (6H)	1.05	3.86
III	0.79	0.87; 1.07	1.25	3.70

*s) singlet; m) multiplet.

SUMMARY

The stereochemistries of three oxides of the bicyclohomofarnesane series have been established by spectral and chemical methods.

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MASS SPECTROMETRY OF NEGATIVE IONS AND THE STEREOCHEMISTRY OF ORGANIC COMPOUNDS.

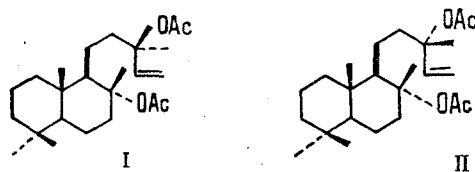
IV. ACETATES OF EPIMERIC DITERPENE GLYCOLS

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In an investigation of the mass spectra of the negative ions (NIs) from the dissociative capture of electrons (DCE) of a series of carbohydrate derivatives, the high stereospecificity of the fragmentation of the molecular NIs of the O-acetates and O-methyl derivatives of the monosaccharides on interaction with low-energy electrons has been established [1-4].

Continuing these investigations with the aim of showing the possibility of using the method of the mass spectrometry of NIs for investigating the stereochemistry of other classes of natural compounds, we have studied the DCE mass spectra of two acetyl derivatives of diterpenoids of the labdane group — the diacetates of sclareol (I) and of 13-episclareol (II) — which are given in Table 1.



It is known that the stereochemical differences of the sclareol and 13-episclareol molecules are connected with the different configurations of the asymmetric atom at C₁₃. Sclareol has the 13-R configuration and episclareol the 13-S configuration [5-10]. Consequently, the question of the influence of such fine differences in the molecules of the diacetates under consideration on the nature of the DCE mass spectra is a matter of interest.

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